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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Ref: **Docket No. 02D-0002; Draft Guidance for Industry "Inhalational Anthrax (Post-Exposure) – Developing Antimicrobial Drugs;** published in the Federal Register on March 18, 2002.

Abbott Laboratories commends the Agency on the efforts to provide guidances for industry for the development of additional therapy for inhalational anthrax. We are very pleased to have the opportunity to comment on the draft guidance "Inhalational Anthrax (Post-Exposure) – Developing Antimicrobial Drugs", March 2002.

We thank the Agency for you consideration of our comments. Should you have any question, please contact MaryClare DeLuca at (847) 936-3374 or by FAX at (847) 937-8002.

Sincerely,

D.L. Sporn by RPlak

Douglas L. Sporn

02D-0002

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Abbott

May 15, 2002

Comments on Draft Guidance for Industry
Inhalational Anthrax (Post-Exposure) –
Developing Antimicrobial Drugs

Docket No. 02D-0002

Abbott Laboratories thanks the Agency for their consideration of the following comments.

III. THE MONKEY MODEL - APPLICABILITY TO THE HUMAN DISEASE

- Lines 178-180: The Agency states, ***"...the Agency believes that the use of the rhesus (macaque) monkey disease and treatment model for inhalational anthrax (post-exposure) provides convincing evidence of efficacy for regulatory purposes."***, *and,*
- Lines 222-223: ***"...as well as convincing evidence from the rhesus monkey model, should be submitted in the application for approval."***

Comments

While we recognize that the best models for humans are non-human primates, rhesus monkey studies should not be a mandatory requirement for the testing of inhalation anthrax. After extensive research performed by Abbott and six other major pharmaceutical companies, there seems to be only one facility in the United States where non-human primate studies with anthrax can be conducted. That facility is the U.S. Army Medical Research Institute of Infectious Diseases (USAMRID), Fort Detrick, MD. The USAMRID project priorities are dictated by the Department of Defense (DOD). Current priorities do not include the testing of antimicrobial drugs on inhalation anthrax, but rather are focused on vaccine studies against viral infections in monkey models. Unlike anthrax studies, which can be performed in other non-human models, monkey models are required for vaccine studies against viral infections. Therefore, no non-human primate studies of anthrax can be done at this time unless the DOD changes their priorities.

There are other non-human models, including rodent models that have been developed. Abbott recommends that the currently published monkey studies conducted by USAMRID with ciprofloxacin, doxycycline and penicillin could be used to bridge to other animal models. By using the monkey data from those studies as a surrogate, a study in another model with the 3 approved drugs and a new drug should be sufficient. One or two models in rodents could be used for evaluation and approval of new drugs for the treatment of inhalation anthrax.

V. INHALATIONAL ANTHRAX (POST-EXPOSURE)

E. Rhesus Monkey And Other Models Of Efficacy

- Line 382: FDA states, ***"Treatment should continue for 30 days."***

Comments

The guidance calls for a 30-day treatment cycle. We believe that a 60-day treatment cycle[1] is necessary followed by 60 days of observation. This would bring the study duration to a total of 120 days.

(1) Inglesby TV, Henderson DA, Bartlett JG, Ascher MS, Eitzen E, Friedlander AM, Hauer J, McDade J, Osterholm MT, O'Toole T, Parker G, Perl TM, Russell PK, Tonat K. *"Anthrax as a biological weapon: medical and public health management."* Working Group on Civilian Biodefense. *JAMA.* 1999 May 12; 281(18): 1735-1745. Review

F. Clinical Pharmacology

- Lines 459-461: FDA states, ***"Full characterization of the metabolic profile (in vitro and in vivo) in humans and in the animals chosen to study the drug for inhalational anthrax (post-exposure) should be provided."***

Comments

We question the relevance of full metabolic profile in rhesus monkeys, since the most current data in many approved antimicrobial drugs were obtained from cynomolgus monkeys. It is unclear if there is any potential difference between the metabolic profiles of cynomolgus and rhesus monkeys. Given that there is a limited number of rhesus or other monkeys (such as African green monkeys) cynomolgus data, the most commonly used species, should be acceptable. Due to the limitations on the supply of monkeys available for research, the priorities should be to use rhesus monkeys and other monkeys for research where there are no other animal models, such as vaccine research. All avenues should be explored to use our available resources for anthrax work.

L. Postapproval Commitments and/or Requirements

- Lines 536-540: FDA states, ***"... the approval letter would request that confirmatory clinical data be provided in the event of an accidental or intentional exposure to aerosolized B. anthracis (§314.510). Applicants should include as part of their application a plan or approach to obtaining such confirmatory data in the event such studies become ethical and feasible as a result of such an exposure".***

Comments

FDA is proposing confirmatory clinical data on all subjects in the event of an accidental or intentional open population exposure. Although it is possible to collect such clinical data in a contained exposure, such as was done in the post office exposures; the collection of such data in an open population would be exceedingly difficult. Given the confidentiality of patient records and prescription records, the question arises as to whether or not industry is ethically allowed to collect such data. It might be more appropriate for public health officials, with funding from industry, to undertake the collection of clinical data. A full public health strategy needs to be developed, with input from CDC, FDA, NIH, medical societies (Infectious Diseases Society of America and others), and industry, in order to have appropriate processes evaluated and ready for implementation should such a need arise in the future.

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